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PAPER

The effect of exercise training on β-adrenergic stimulation of fat metabolism in obese men

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OBJECTIVE: To investigate the *in vivo* effect of exercise training at high and low intensity on β-adrenergic stimulated fat metabolism in obese men at rest.
METHOD: Twenty-three obese, healthy subjects were randomly divided in a low-intensity exercise training program (40% VO_{2max}, $n=7$), a high-intensity exercise training program (70% VO_{2max}; $n=8$), or a non-exercising control group ($n=8$). The exercise training program lasted for 12 weeks with a training frequency of 3 times per week. Before and after the intervention body composition and maximal aerobic capacity were measured as well as fat metabolism at rest and during β-adrenergic stimulation by isoprenaline. For comparison, six lean subjects served as a control group. They participated in a low-intensity exercise training program and underwent the same measurements as the obese subjects.
RESULTS: Relative fat oxidation decreased significantly during infusion of an increasing dose of isoprenaline in the obese low-intensity and high-intensity exercise training groups as well as in the lean group ($P<0.01$). Exercise training failed to influence the effect of β-adrenergic stimulation on relative fat oxidation in obese men at both intensities and in lean men. In addition, β-adrenergic-mediated lipolysis did not seem to be different after low intensity exercise training in lean and obese men. Lipolysis might be increased after high-intensity exercise training in obese men.
CONCLUSION: Low- and high-intensity exercise training in obese men failed to affect β-adrenergic mediated relative fat oxidation *in vivo*. β-Adrenergic-mediated lipolysis might be increased in obese men after HI exercise training only. The effect of low-intensity exercise training on β-adrenergic-mediated fat metabolism was similar in lean and obese men.
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Keywords: low-intensity exercise; isoprenaline; respiratory exchange ratio; lipolysis; sympathetic nervous system

Introduction

Obese subjects appear to have an impaired catecholamine-induced lipolysis.[1,2] *In vitro* lipolysis studies suggest that this may be due to an increased α_2-adrenergic and a decreased β-adrenergic lipolytic response in obese compared to lean men.[3] The decreased β-adrenergic response was associated with a decreased expression of β_2-adrenoceptors in obese women.[4] *In vivo* β-adrenergic stimulation increased relative fat oxidation (fat oxidation relative to total energy expenditure) in lean subjects but failed to increase relative fat oxidation in obese subjects.[1,2,5,6] Obese subjects seem to have an impaired utilization of FFA in the muscle.[7] Furthermore, a positive correlation has been reported between 24-h fat oxidation and β-adrenergic sensitivity in Pima Indian males[8] and between an impaired β-adrenergic mediated lipolysis *in situ* and a low basal fat oxidation rate.[9] Together these data suggest that β-adrenergic stimulation of lipolysis and fat oxidation is impaired in the obese. Endurance exercise training is known to increase the rate of fat oxidation during exercise and maybe also at rest.[10–15] In a previous study we found that low-intensity exercise training increased fat oxidation during exercise in obese subjects.[16] Several cross-sectional *in vitro* studies have shown that the sensitivity of abdominal adipocytes to the lipolytic action of catecholamines is increased in lean endurance-trained compared to sedentary individuals.[17–22] This effect seems to be related to the increased response of the β-adrenergic pathway[20–22] and possibly also to a decreased response of the α_2-adrenergic

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pathway to a fixed stimulus.[21,22] On the other hand, a cross-sectional study using *in situ* microdialysis showed no difference in lipolytic sensitivity to adrenaline between trained and untrained lean men.[23]

Since β-adrenergic-stimulated lipolysis and fat oxidation are impaired in obese subjects, the effect of exercise training on β-adrenergic stimulated fat metabolism in obese is not necessarily similar to the effects in lean subjects. To our knowledge, only one study investigated the effect of moderate-intensity exercise training on isoprenaline-induced lipolysis in obese subjects *in vitro*[24] and *in situ* by the microdialysis technique.[25] These investigators reported an increased β-adrenergic stimulated lipolysis after exercise training. However, no data are available on the effect of exercise training on *in vivo* β-adrenergic-stimulated fat metabolism in obese subjects. Therefore, the present study was undertaken to investigate the effect of exercise training at different intensities on *in vivo* β-adrenergic stimulated lipolysis and fat oxidation in obese male subjects.

Methods

Subjects

Twenty-three obese male subjects participated in the present study. Physical characteristics of the subjects are indicated in Table 1. All subjects were in good health as assessed by medical history and physical examination. They did not take medication known to influence the variables measured and had a stable body weight (<3 kg change) during 2 months prior to selection. They did not spend more than 2 h per week in sports activities and had no physically demanding job. Subjects were matched in groups of three for age, BMI, fat percentage and maximal oxygen uptake per kg fat free mass (VO_{2max}/kg FFM). Subsequently members of each group were randomly divided over three groups, the low-intensity (LI) or high-intensity (HI) exercise training group and the control group (C). Subjects were requested to maintain their dietary habits during the study. The study protocol was approved by the Ethics Committee of Maastricht University. Written informed consent was obtained from all subjects.

Experimental design

Two of the three obese groups participated in the exercise training program for 12 weeks. The third group served as a non-training control group (C). Measurements of body composition, maximal aerobic capacity and isoprenaline-induced thermogenesis and substrate oxidation were made before the start of the exercise training program and within 1 week after 12 weeks of exercise training (36–86 h after the last exercise bout). The exercise training program was continued until all measurements were performed.

Exercise training

The exercise training program consisted of cycling on an ergometer (Bodyguard Cardiocycle, Sandnes, Norway or Lode, Groningen, The Netherlands) at either low intensity (LI; 40% VO_{2max}) or high intensity (HI; 70% VO_{2max}). Seven obese subjects participated in the LI and eight obese subjects in the HI training program. Subjects trained for 12 weeks, three times per week. Energy expenditure of each subject in each training session was fixed at 5 kcal · kg FFM^{-1}. Training duration for obese subjects in the LI and HI training program during the first month was 57.1 ± 8.0 and 32.8 ± 2.5 min per session, respectively. Heart rate was monitored continuously during the training sessions (Polar Electro, Oy, Finland). After 4 and 8 weeks of exercise training, a maximal aerobic exercise test was performed and the training workload and duration were adjusted if necessary. All training sessions took place at the laboratory under supervision of a professional trainer.

Lean control group

As no data were available in the literature on the effect of exercise training on *in vivo* β-adrenergic-mediated fat metabolism in lean subjects, besides the obese group a lean group was also included in the study. In this group six men participated. They were all lean (percentage fat ≤24) and matched for age with the obese group. They did not spend more than 2 h a week in sports activities and had no physically demanding job. All subjects participated in the LI

Table 1 Subject characteristics (mean ± s.d.) in obese ($n = 23$) and lean ($n = 6$) subjects before (1) and after (2) the exercise training period in the low-intensity training group (LI), high-intensity training group (HI) and the control group (C)

	Obese LI (1)	Obese LI (2)	Obese HI (1)	Obese HI (2)	Obese C (1)	Obese C (2)	Lean LI (1)	Lean LI (2)
Age (y)	42.9 ± 6.6		40.0 ± 6.3		43.3 ± 5.4		42.7 ± 4.9	
Body weight (kg)	102.7 ± 10.8	103.1 ± 11.4	105.5 ± 6.6	105.1 ± 6.2	96.5 ± 10.3	95.9 ± 9.6	71.4 ± 6.8[c]	70.3 ± 7.1
BMI ($kg \cdot m^{-2}$)	31.1 ± 3.0	31.3 ± 3.1	32.2 ± 1.6	32.1 ± 1.3	31.5 ± 2.4	31.4 ± 2.5	22.7 ± 2.5[c]	22.3 ± 2.4
Fat percentage (%)	32.3 ± 2.3	31.9 ± 2.1	31.3 ± 4.3	31.8 ± 4.4	31.6 ± 5.1	31.7 ± 5.0	17.9 ± 4.3[c]	17.5 ± 4.1
VO_{2max} ($ml \cdot min^{-1}$)	3191 ± 532	3556 ± 542[a]	3312 ± 4448	3820 ± 453[ab]	2944 ± 443	3019 ± 557	3223 ± 424	3293 ± 220
VO_{2max} FFM ($ml \cdot kg^{-1} \cdot min^{-1}$)	45.7 ± 5.9	51.6 ± 4.9[a]	45.6 ± 3.2	53.3 ± 3.7[ab]	44.6 ± 3.3	45.8 ± 3.3	55.2 ± 6.1[d]	57.1 ± 3.3

[a]Significantly different from before; $P < 0.05$.
[b]Change significantly different from C group; $P < 0.05$.
[c]Significantly different from obese LI (1); $P < 0.01$.
[d]Significantly different from obese LI (1); $P < 0.05$.

exercise training program and trained on average for 47.5 ± 6.0 min per session (energy expenditure 5 kcal · kg FFM^{-1}) with the same frequency as the obese group. The training and measurement protocol were the same as described for the obese group.

Measurements

Body composition. Body density was measured by hydrostatic weighing, with a correction for residual lung volume estimated by helium dilution with a spirometer (Volugraph 2000, Mijnhardt, The Netherlands) at the moment of underwater weighing. Body composition was calculated according to the formula of Siri.[26]

Maximal aerobic capacity. Maximal O_2 uptake (VO_{2max}) for each subject was determined by an incremental exercise test on an electromagnetically braked cycle ergometer (Lode, Groningen, The Netherlands). After a warming up period of 5 min at 100 W, workload was increased every 4 min by 40 W until exhaustion. During the experiment ventilatory and gas exchange responses were measured continuously, using indirect calorimetry (Oxycon β, Mijnhardt, The Netherlands). Heart rate was recorded continuously by an electrocardiogram. The highest oxygen uptake achieved over 30 s was taken as VO_{2max}.

Isoprenaline infusion test. An isoprenaline (ISO) infusion test was performed before and after the exercise training program to determine the effect of exercise training on β-adrenergically mediated thermogenic, metabolic and heart rate (HR) responses. The protocol of this test has been described previously.[1] The experiments were mostly performed 38 h (at least 36 h and at maximum 86 h) after the last exercise bout in a room with a temperature between 23 and 25°C. After an overnight fast, subjects came to the laboratory by car or bus. Catheters were inserted in a right and left forearm vein for infusion of the nonselective β-adrenoceptor agonist ISO and for blood sampling. The subjects remained in semi-supine position throughout the experiment. After a 30-min baseline measurement period, ISO was infused by a Harvard syringe pump in increasing doses of 6, 12 and 24 ng · kg fat-free $mass^{-1} \cdot min^{-1}$, each dose for 30 min. The dose is related to ISO sulphate, 69% of which corresponds to ISO free base. During the experiment blood pressure was recorded every 5 min and HR was recorded continuously by an electrocardiogram. When HR had risen 30 beats/min or more, infusion was stopped.

At the end of the baseline period and of each infusion period a blood sample was taken. During the whole experiment expired CO_2, inspired O_2 and respiratory exchange ratio (RER) were determined by an open circuit ventilated hood system (Oxycon β, Mijnhardt, The Netherlands). The accuracy of the ventilated hood system for gas exchanges was tested regularly and verified to be within 5%. Energy expenditure was calculated according to the formula of Weir.[27] RER values reached a steady state after 20 min infusion. RER, EE and HR were averaged over the last 10 min of each infusion period.

Biochemical analysis. After blood sampling, blood was put into an EDTA-containing chilled 10 ml tube (for analysis of FFA, glucose, insulin and glycerol) or a heparin-containing 10 ml tube with 300 µl glutathione (45 µg/l saline) (for analysis of ISO). Blood was immediately centrifuged for 10 min at 3000 rpm at 4°C and plasma was stored at −80°C.

Analyses of plasma concentrations FFA (NEFA C kit; Wako Chemicals, Neuss, Germany), glycerol (Glycerol kit; Boehringer, Mannheim, Germany) and lactate[28] were performed on a COBAS FARA centrifugal spectrophotometer. Plasma glucose concentrations (GLUC HK kit; Hoffmann-La Roche, Basel, Switzerland) were measured on a COBAS BIO centrifugal spectrophotometer. Plasma insulin concentrations were measured with a double-antibody radioimmunoassay (Insulin RIA 100; Pharmacia, Uppsala, Sweden). Plasma isoprenaline concentrations were analysed by HPLC with electrochemical detection.[29]

Statistical analysis

Values were expressed as means ± standard deviations. A Friedman test was performed to detect changes due to the ISO dose infused. All values were corrected for baseline values and the mean effect over all time points was calculated for each subject. Exercise training effects on the calculated mean values within a group were analysed by a Wilcoxon signed-rank test. A Kruskal–Wallis test was performed to test differences in initial values and changes due to the intervention among the three obese groups. *Post hoc* testing was done by the Mann–Whitney test. Where appropriate, *P*-values of the *post hoc* comparisons were corrected according to Bonferroni inequalities. A Mann–Whitney test was used to compare the initial values between lean and obese and lean and the obese LI group and to test changes due to the intervention between lean and the obese LI group. A *P*-value smaller than 0.05 was regarded as statistically significant.

Results

Subject characteristics

After the intervention body composition was not changed in any group (Table 1). VO_{2max} and VO_{2max} FFM were significantly improved in the obese LI and HI exercise groups ($P < 0.05$), but not in the lean LI and obese C group. The change in VO_{2max} and VO_{2max} FFM were not significantly different between the LI and the HI exercise group, but significantly different between the HI and C group ($P < 0.01$ and $P < 0.05$, respectively). Attendance at the exercise training sessions was 88.7 ± 8.7% for the LI group and 92.6 ± 5.5% for the HI group.

Effect of exercise training on β-adrenergic stimulation of fat metabolism in obese

Before the intervention, infusion of an increasing dose of ISO decreased respiratory exchange ratio (RER) significantly ($P < 0.01$) in the obese LI and HI groups, but not in the C group (Figure 1). However, average ISO-induced effect on RER before the intervention was not significantly different among the three obese groups. None of the interventions affected the ISO-induced decrease in RER significantly.

Basal energy expenditure and heart rate were not significantly different among the obese groups before the intervention (Table 2). Infusion of ISO significantly increased energy expenditure ($P < 0.01$; Figure 2) and heart rate ($P < 0.001$; Figure 3). The effect of ISO on energy expenditure and heart rate was not influenced by any of the interventions. Infusion of ISO significantly increased plasma FFA, insulin, lactate and glycerol concentrations ($P < 0.05 - 0.001$) and significantly decreased plasma glucose concentrations ($P < 0.05 - 0.01$; Table 3). Basal plasma concentrations before the intervention were not significantly different among groups and did not change due to the intervention (Table 2). HI exercise training only increased the effect of ISO on plasma glycerol concentration significantly ($P < 0.05$; Figure 4), but did not affect plasma FFA concentrations (Figure 5). In the LI and C group, the ISO-induced increase in plasma glycerol and FFA concentrations after the intervention were not different from before. None of the interventions affected the ISO-induced changes in plasma glucose, insulin or lactate concentrations (Table 3).

Effect of LI exercise training on β-adrenergic mediated fat metabolism in obese *vs* lean subjects

Baseline values for body weight, BMI and fat percentage were significantly lower in the lean group compared to the obese LI group ($P < 0.01$; Table 1). Baseline VO_{2max} was not different between the lean and obese group. However, expressed per kg FFM the lean group showed higher values ($P < 0.05$). The increase in VO_{2max} due to exercise training

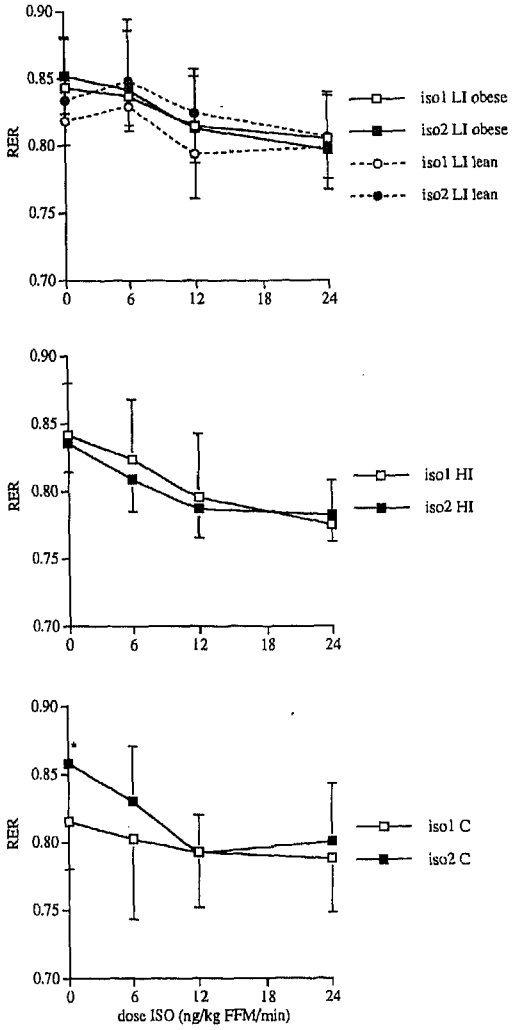

Figure 1 RER during increasing dose of isoprenaline (ISO) infusion before (1) and after (2) exercise training in the low intensity (LI) lean ($n = 6$) and obese group (1A) ($n = 7$) and the obese high-intensity (HI) (1B) ($n = 8$) and control (C) (1C) ($n = 8$) group. *Significantly different from before; $P < 0.05$.

Table 2 Baseline values (mean ± s.d.) for heart rate (HR), energy expenditure (EE), respiratory exchange ratio (RER) and plasma metabolites in the obese low-intensity (LI) and high-intensity (HI) training group, the obese control (C) group and the lean LI group before (1) and after (2) the intervention

	Obese LI (1)	*(2)*	*HI (1)*	*(2)*	*C (1)*	*(2)*	*Lean LI (1)*	*(2)*
HR (beats · min^{-1})	66 ± 11	63 ± 7	60 ± 9	58 ± 8	68 ± 12	66 ± 12	59 ± 5	59 ± 8
EE (kJ · min^{-1})	5.84 ± 0.94	6.10 ± 0.91	6.35 ± 0.67	6.16 ± 0.61	6.07 ± 0.73	5.89 ± 0.58	4.83 ± 0.41[c]	4.92 ± 0.57
EE/FFM (J · min^{-1} · kg^{-1})	85 ± 10	87 ± 6	87 ± 9	86 ± 6	93 ± 14	91 ± 14	83 ± 4	86 ± 11
RER	0.84 ± 0.02	0.85 ± 0.03	0.84 ± 0.04	0.84 ± 0.02	0.82 ± 0.04	0.86 ± 0.04[a]	0.82 ± 0.02	0.83 ± 0.05
FFA (μmol · l^{-1})	453 ± 236	368 ± 175	361 ± 139	394 ± 77	530 ± 193	383 ± 126	376 ± 84	239 ± 85[a]
glycerol (μmol · l^{-1})	75.6 ± 33.3	67.9 ± 17.8	76.1 ± 21.1	61.7 ± 13.5	81.3 ± 22.6	66.5 ± 19.5	68.5 ± 22.0	49.7 ± 18.0
glucose (mmol · l^{-1})	5.23 ± 0.38	5.32 ± 0.57	5.47 ± 0.41	5.51 ± 0.34	5.55 ± 0.68	5.64 ± 0.56	4.85 ± 0.49[b]	5.09 ± 0.55
insulin (μU · ml^{-1})	12.3 ± 5.8	12.7 ± 5.0	12.4 ± 5.6	11.9 ± 4.4	9.1 ± 3.2	12.3 ± 7.4	4.53 ± 1.20[c]	4.84 ± 1.08
lactate (mmol · l^{-1})	1.02 ± 0.44	1.13 ± 0.27	0.89 ± 0.29	0.95 ± 0.17	0.94 ± 0.28	0.95 ± 0.19	0.61 ± 0.12[c]	0.75 ± 0.26

[a]Significantly different from before; $P < 0.05$.
[b]Significantly different from obese; $P < 0.05$.
[c]Significantly different from obese; $P < 0.01$.

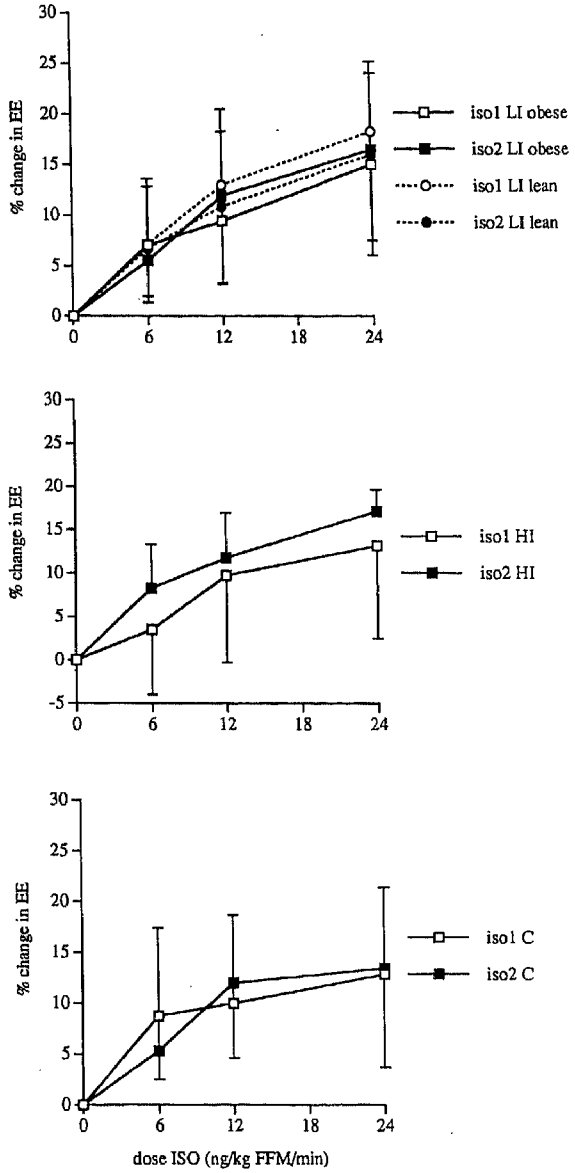

Figure 2 Percentage change in energy expenditure (EE) from basal before (1) and after (2) exercise training in the low-intensity (LI) lean ($n=6$) and obese group (1A) ($n=7$) and the obese high-intensity (HI) (1B) ($n=8$) and control (C) (1C) ($n=8$) group.

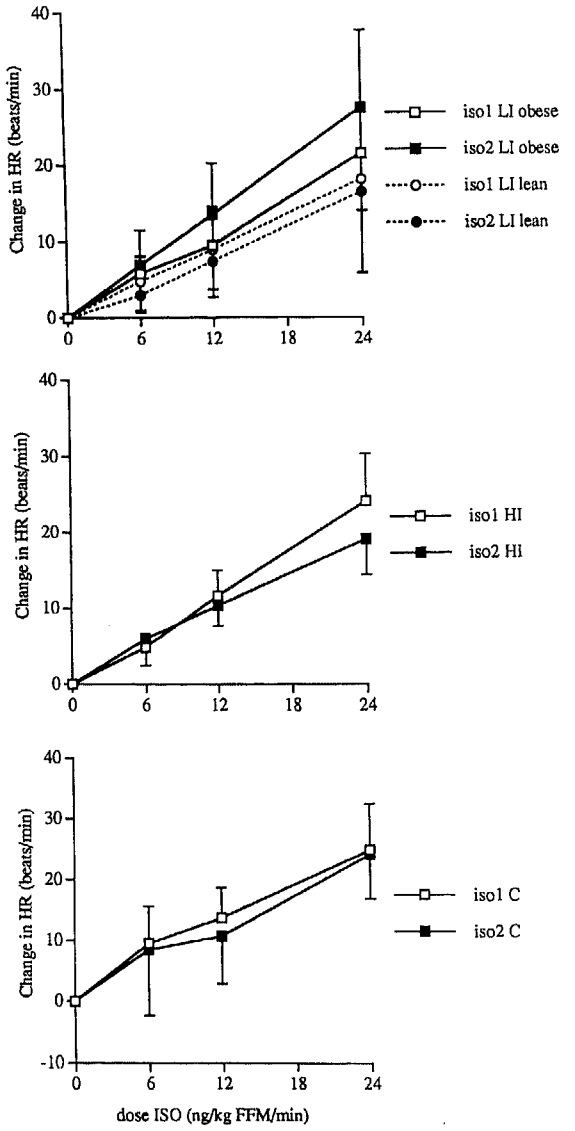

Figure 3 Change in heart rate (HR) (beats/min) from basal before (1) and after (2) exercise training in the low-intensity (LI) lean ($n=6$) and obese group (1A) ($n=7$) and the obese high-intensity (HI) (1B) ($n=8$) and control (C) (1C) ($n=8$) group.

was significantly greater in the obese LI group compared to the lean LI group ($P<0.05$) and VO_{2max}/FFM showed a similar tendency ($P=0.06$). Attendance at the exercise training sessions by lean subjects was $85.7\pm10.4\%$.

Before the intervention, infusion of ISO did not decrease RER significantly in the lean group (Figure 1). However, resting RER (Table 2) and the ISO-induced decrease in RER in lean subjects were not significantly different from those in obese subjects. Exercise training had no effect on ISO-induced decrease in RER in the lean group as in the obese LI group. Basal energy expenditure in lean subjects was significantly lower than in obese subjects ($P=0.001$), but not when adjusted for fat-free mass (Table 2). Infusion of ISO significantly increased energy expenditure ($P<0.001$; Figure 2) and heart rate ($P<0.001$; Figure 3). The ISO-induced increase in energy expenditure and heart rate was not different before and after LI exercise training in lean and obese subjects.

Before the intervention basal plasma concentrations of lactate ($P<0.01$), glucose ($P<0.05$) and insulin ($P=0.001$) were significantly lower in the lean group compared to the obese (Table 2). The intervention did not affect basal plasma concentrations, except for the basal FFA concentration

Table 3 Average ISO-induced change (mean ± s.d.) in plasma metabolite concentrations in the obese LI, HI and C group and the lean LI group before (1) and after (2) the intervention

	Obese LI (1)	*(2)*	*HI (1)*	*(2)*	*C (1)*	*(2)*	*Lean LI (1)*	*(2)*
FFA (μmol/l)	313 ± 133[a]	450 ± 130[a]	368 ± 171[a]	416 ± 117[a]	223 ± 172[c]	342 ± 201[a]	384 ± 179[a]	321 ± 128[a]
Glycerol (μmol/l)	27.7 ± 12.0[b]	46.6 ± 30.0[a]	27.9 ± 28.3[a]	53.6 ± 18.0[ad]	22.6 ± 26.3	32.9 ± 30.8[b]	41.2 ± 19.6[a]	26.1 ± 20.5[c]
Glucose (mmol/l)	−0.48 ± 0.64[c]	−0.16 ± 0.31	−0.25 ± 0.14[b]	−0.32 ± 0.29[c]	−0.67 ± 0.88[b]	−0.28 ± 0.21[b]	−0.17 ± 0.08[b]	−0.27 ± 0.17[b]
Insulin (μU/ml)	5.0 ± 3.8[b]	7.0 ± 2.7[a]	4.9 ± 3.2[a]	5.1 ± 2.2[b]	3.4 ± 2.4[b]	7.3 ± 4.2[cd]	2.4 ± 1.9[b]	2.3 ± 0.8[b]
Lactate (mmol/l)	0.09 ± 0.15	0.09 ± 0.15[c]	0.10 ± 0.18[c]	0.09 ± 0.10[c]	− 0.01 ± 0.18	0.03 ± 0.11	0.06 ± 0.08[c]	0.09 ± 0.05[b]

[a]Significantly change versus baseline; $P < 0.001$.
[b]Significantly change versus baseline; $P < 0.01$.
[c]Significantly change versus baseline; $P < 0.05$.
[d]Significantly different from before; $P < 0.05$.

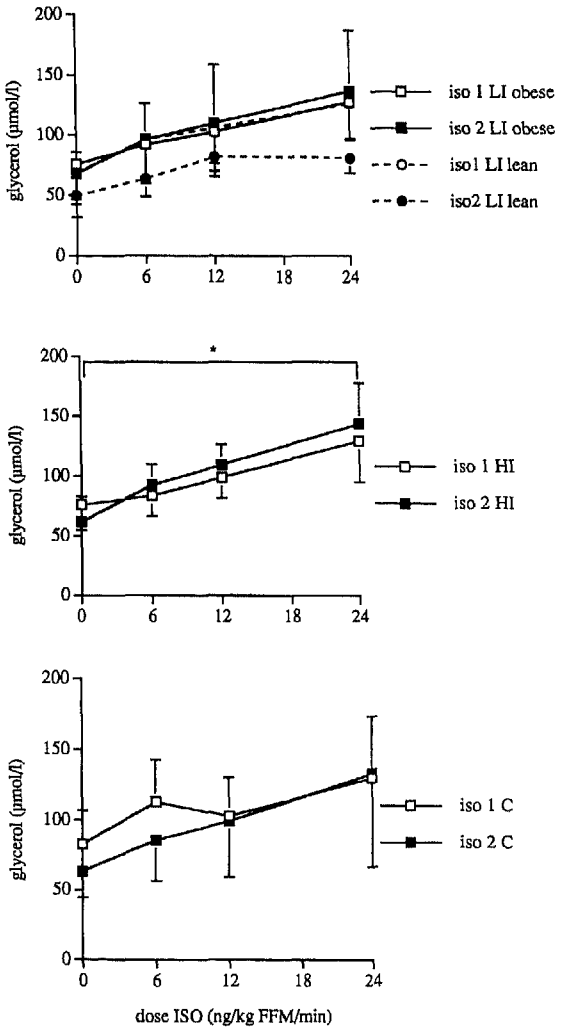

Figure 4 Plasma glycerol concentrations (μmol/l) before (1) and after (2) exercise training in the low-intensity (LI) lean ($n = 6$) and obese group (1A) ($n = 7$) and the obese high-intensity (HI) (1B) ($n = 8$) and control (C) (1C) ($n = 8$) group. *Average increase significantly different from before, $P < 0.05$.

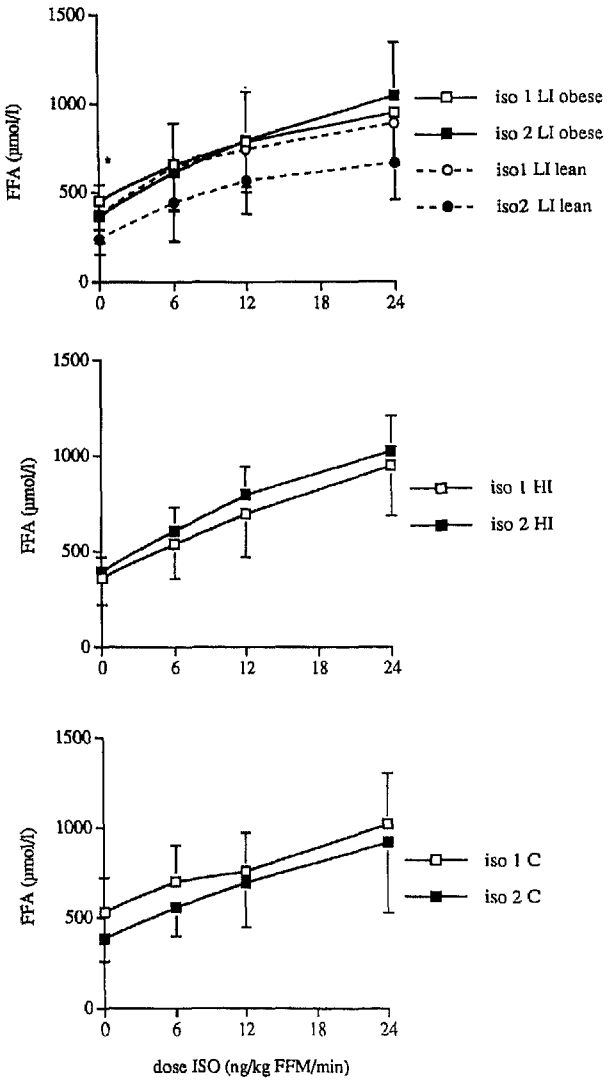

Figure 5 Plasma FFA concentrations (μmol/l) before (1) and after (2) exercise training in the low-intensity (LI) lean ($n = 6$) and obese group (1A) ($n = 7$) and the obese high-intensity (HI) (1B) ($n = 8$) and control (C) (1C) ($n = 8$) group. *LI lean significantly different from before; $P < 0.05$.

which decreased due to the intervention ($P < 0.05$). ISO-induced changes in plasma concentrations before the intervention were not significantly different between the lean and obese group (Table 3). LI exercise training did not influence the effect of ISO on plasma concentrations either in obese or in lean subjects (Table 3).

Discussion

The main finding of the present study was that neither low- nor high-intensity exercise training in obese men increased the sensitivity to *in vivo* β-adrenergic stimulation with respect to RER, EE, HR and plasma metabolites. However, also in lean subjects, LI exercise training failed to affect β-adrenergic sensitivity *in vivo*.

The present study was designed to investigate whether the impaired sympathetically mediated fat oxidation, reported in obese subjects in several studies,[1,5,6,30] could be improved by exercise training independent of changes in body mass and body composition. However, the obese subjects who participated in the present study did not appear to have a blunted β-adrenergically mediated fat oxidation. Infusion of ISO in an incremental dose increased relative fat oxidation in obese subjects ($P < 0.01$). This effect was in agreement with that previously found in lean.[1,5,6,30] Apparently the effect of β-adrenergic stimulation on fat oxidation is variable in obese subjects. Unfortunately no data were available to compare the level of physical fitness of the obese subjects in our study with the obese subjects in the studies mentioned above. However, it is possible that the obese subjects in the present study, who volunteered in an exercise training program, were better trained than the average obese subject participating in other non-training studies.[1,5,6,30] It is known in the lean that exercise-trained subjects have an increased β-adrenergic lipolytic response *in vitro* compared to sedentary subjects.[17,19–22,31] Moreover, also variations in habitual energy expenditure seem to play a role in the difference between high and low responders of β-adrenergic adipocyte lipolysis.[31]

In the present study exercise training in obese subjects was not effective in increasing the effect of *in vivo* β-adrenergic stimulation on relative fat oxidation. Nevertheless, exercise training sessions were well attended (about 90%) and physical fitness improved in both the obese LI and the HI exercise training groups. Moreover, the failure to improve β-adrenergic sensitivity did not seem to be biased by concentration differences of ISO in plasma before and after the intervention, which were not significantly different (highest dose 278 ± 64 ng/l before and 255 ± 46 ng/l after the intervention in the HI group).

Data on plasma metabolites are in agreement with the failure to improve ISO-stimulated relative fat oxidation by exercise training. The effect of ISO infusion on plasma metabolites was similar before and after exercise training, except for the concentration glycerol in the HI group, which increased more after the intervention ($P < 0.05$). This might indicate that HI exercise training slightly increased β-adrenergic mediated lipolysis in obese. Another study in obese subjects reported an increased ISO-stimulated FFA and glycerol response after moderate- to high-intensity exercise training,[25] while fat mass and fat-free mass were not changed. They also found an increased β-adrenergic stimulated lipolytic activity in subcutaneous adipose tissue. In adipocytes, training also has been shown to enhance the β-adrenergic lipolytic response and to blunt the antilipolytic effect of insulin and α_2-adrenoceptor stimulation.[24] However, these experiments were performed *in vitro* and *in situ*. *In vitro* measurement of fat cell lipolysis can not be used to directly predict *in vivo* FFA metabolism, due to the different environment of metabolites and hormones of the adipose cell *in vivo* compared to *in vitro*.[32]

In the present study β-adrenergic stimulation significantly increased heart rate ($P < 0.001$). Exercise training did not influence this effect, which is in agreement with data on epinephrine infusion in lean trained and untrained subjects.[23]

As in the obese subjects, exercise training did not affect *in vivo* stimulated β-adrenergic fat metabolism in the lean subjects in the present study either. Another study showed an increased whole body lipid oxidation during epinephrine infusion in trained compared to untrained subjects,[23] but the discrepancy in training state between trained and untrained was much higher in that study compared to ours. Another factor confounding the comparison is that in that study of Stallknecht *et al*[23] the sympathetic nervous system was activated by epinephrine (α- and β-agonist) while in the present study only a β-agonist was used.

Since the effect of ISO infusion on plasma metabolite concentrations was not changed in lean subjects in the present study, exercise training did not seem to affect β-adrenergic-mediated lipolysis. However, cross-sectional *in vitro* studies in lean subjects found an increased adipocyte lipolytic response in lean trained subjects compared to untrained, which could be explained by an increased β-adrenergic sensitivity[18,20,22] and a decreased α-adrenoceptor sensitivity.[22] On the other hand, another study found no difference in epinephrine-stimulated *in situ* lipolysis in adipose tissue of lean trained and untrained subjects.[23]

In the present study indirect methods were used to determine lipolysis (plasma glycerol and FFA) and fat oxidation (RER). Confirmation of the results with more direct techniques (eg [U-^{13}C]palmitate infusion and microdialysis) is desirable and can be suggested for future research.

In summary, the present study demonstrated that 12 weeks of exercise training in obese subjects at either high or low intensity did not affect *in vivo* β-adrenergic stimulation of relative fat oxidation. Beta-adrenergic-mediated lipolysis might be increased after HI exercise training in obese subjects. The effect of low-intensity exercise training on ISO-induced fat metabolism was similar in lean and obese men.

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